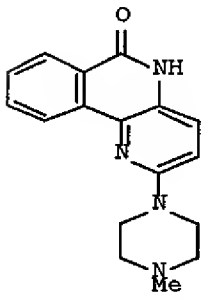
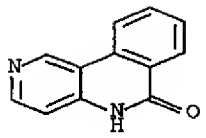
L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:444234 CAPLUS
DN 139:179959
TI Design and Synthesis of Poly ADP-ribose Polymerase-1 Inhibitors. 2. Biological Evaluation of Aza-5[H]-phenanthridin-6-ones as Potent, Aqueous-Soluble Compounds for the Treatment of Ischemic Injuries
AU Ferraris, Dana; Ko, Yao-Sen; Pahutski, Thomas; Ficco, Rica Pargas; Serdyuk, Larisa; Alemu, Christina; Bradford, Chadwick; Chiou, Tiffany; Hoover, Randall; Huang, Shirley; Lautar, Susan; Liang, Shi; Lin, Qian; Lu, May X.-C.; Mooney, Maria; Morgan, Lisa; Qian, Yongzhen; Tran, Scott; Williams, Lawrence R.; Wu, Qi Yi; Zhang, Jie; Zou, Yinong; Kalish, Vincent
CS Guilford Pharmaceuticals Inc., Baltimore, MD, 21224, USA
SO Journal of Medicinal Chemistry (2003), 46(14), 3138-3151
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 139:179959
GI



I

AB Aza-5[H]-phenanthridin-6-ones such as the dimesylate salt of I are prepd. as inhibitors of poly ADP-ribose polymerase-1 (PARP-1) for the treatment of ischemic injuries. The inhibitory potency of unsubstituted aza-5[H]-phenanthridin-6-ones (i.e., benzonaphthyridones) depends on the position of the nitrogen atom within the core structure; A ring nitrogen analogs (7-, 8-, and 10-aza-5[H]-phenanthridin-6-ones) are an order of magnitude less potent than C ring nitrogen analogs (1-, 2-, 3-, and 4-aza-5[H]-phenanthridin-6-ones). 2-Substituted 1-aza-5[H]-phenanthridin-6-ones are designed to improve the soly. and pharmacokinetic profiles for azaphenanthridone PARP-1 inhibitors. Three compds. from this series demonstrated statistically significant protective effects in rat models of stroke and heart ischemia; in particular, the dimesylate salt of I reduces damage in rats caused by cerebral and myocardial infarction.
IT **53439-83-1P**, Benzo[c][1,6]naphthyridin-6(5H)-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of azaphenanthridones as inhibitors of poly ADP-ribose polymerase-1 for the treatment of heart and brain ischemia-related injury and the soly. and pharmacol. of selected inhibitors)
RN 53439-83-1 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one (9CI) (CA INDEX NAME)

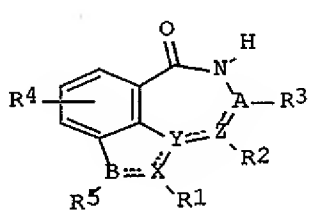


RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:428911 CAPLUS
DN 137:6205
TI Preparation of benzazepinones, isoquinolinones and related compounds as inhibitors of poly(ADP-ribose) polymerase (PARP) for the prevention and/or treatment of tissue damage from cell trauma or cell death due to necrosis or apoptosis.
IN Ferraris, Dana V.; Li, Jia-He; Kalish, Vincent J.; Zhang, Jie
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002044183	A2	20020606	WO 2001-US44815	20011130
	WO 2002044183	A3	20030522		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002036521	A5	20020611	AU 2002-36521	20011130
	US 2003022883	A1	20030130	US 2001-996776	20011130
	EP 1339402	A2	20030903	EP 2001-986053	20011130
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-250132P	P	20001201		
	US 2001-310274P	P	20010809		
	WO 2001-US44815	W	20011130		

OS MARPAT 137:6205
GI



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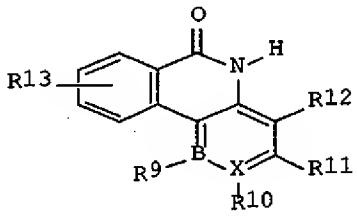

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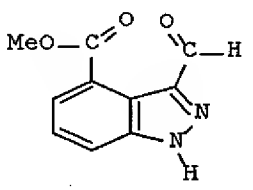

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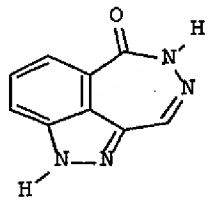


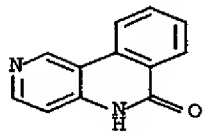
IV

AB This invention discloses the prepn. of title compds. I and II, their pharmaceutically acceptable salts, and related compds. as inhibitors of poly(ADP-ribose) polymerase (PARP) [wherein: A = N, C, CH2, CH; B = C, N, NH, S, SO, SO2; X = C, CH, N; Y = C, N; Z = C, CH2, N, CO; provided

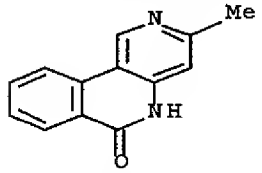
that at least one of X, Y, or Z is N; R1, R2, R3, R5 when present are optionally or independently = H, OH, :O, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, carboxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, halogen, amine, COR8 (R8 = H, OH, (un)substituted alkyl, alkenyl, alkynyl,alkoxy, carboxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl), OR6, NR6R7 (R6, R7 independently = H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl); R1, R2, R3, R5 optionally form ring through a straight or branched C1-4alkyl which may addnl. contain 1-2 double or triple bonds; R4 = 1-3 of H, halo, or alkyl; with proviso that when A, X, or Z = C, then R1, R2, R3 when present may also independently = halogen, CN, O; R9, R10, R11, R12 optionally or independently = H, halogen, amino, OH, halo-amine, O-alkyl, O-aryl, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, carboxy, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, COR8; R13 = 1-3 of H, halogen, alkoxy, alkyl]. For example, cyclocondensation of formylindazole III (prepd. from Me indole-4-carboxylate and NaNO2/AcOH), with hydrazine provided claimed benzoazulenone IV as a white solid. Benzoazulenone IV inhibited human recombinant PARP at an IC50 of 0.018 .mu.M. PARP IC50 inhibition studies for an addnl. 156 examples are provided, ranging in values from 0.01 to 20 .mu.M. Biol. data are provided for the in vivo treatment of focal cerebral ischemia and gout via PARP inhibition with selected compds. II. The present invention is believed to protect cells, tissue and organs against the ill-effects of reactive free radicals and nitric oxide through inhibition of PARP activity.

IT **53439-83-1P**, Benzo[c][1,6]naphthyridin-6(5H)-one
433726-91-1P 433726-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(drug candidate; prepn. of benzazepinones, isoquinolinones and related compds. as inhibitors of poly(ADP-ribose) polymerase (PARP))

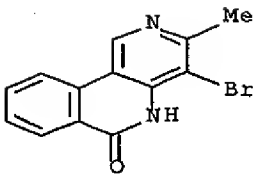
RN 53439-83-1 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one (9CI) (CA INDEX NAME)



RN 433726-91-1 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one, 3-methyl- (9CI) (CA INDEX NAME)



RN 433726-92-2 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one, 4-bromo-3-methyl- (9CI) (CA INDEX NAME)


N
Me
Br
NH
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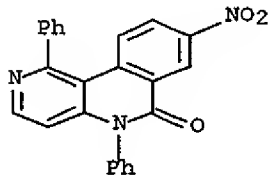
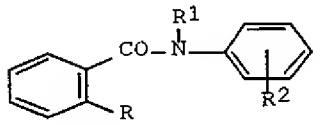
L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:924689 CAPLUS
DN 136:309831
TI Enaminone acylation: competitive formation of quinolin-4-one and isoquinolin-1-one derivatives
AU Vales, Magali; Lokshin, Vladimir; Pepe, Gerard; Samat, Andre; Guglielmetti, Robert
CS Universite de la Mediterranee, Faculte des Sciences de Luminy, UMR 6114 CNRS, Marseille, 13288, Fr.
SO Synthesis (2001), (16), 2419-2426
CODEN: SYNTBF; ISSN: 0039-7881
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 136:309831
AB The reaction of enaminones with some o-halobenzoyl chlorides allows the prepn. of 2-acyl-2-alkylquinolin-4-one and/or 4-acyl-3-alkylisoquinolin-1-one derivs. depending on the structure of the starting materials. Due to their easy availability the compds. prepd. are attractive precursors for further synthesis of polycondensed heterocycles.
IT **411231-86-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(enaminone acylation and competitive formation of quinolin-4-one and isoquinolin-1-one derivs.)
RN 411231-86-2 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one, 8-nitro-1,5-diphenyl- (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

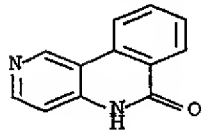
L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:162346 CAPLUS
DN 134:359384
TI Photoreaction of 2-Halo-N-pyridinylbenzamide: Intramolecular Cyclization Mechanism of Phenyl Radical Assisted with n-Complexation of Chlorine Radical
AU Park, Yong-Tae; Jung, Chang-Hee; Kim, Moon-Sub; Kim, Kwang-Wook; Song, Nam Woong; Kim, Dongho
CS Department of Chemistry, Kyungpook National University, Taegu, 702-701, S. Korea
SO Journal of Organic Chemistry (2001), 66(7), 2197-2206
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
GI



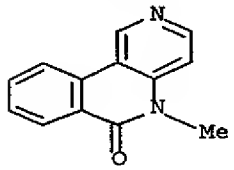
I

AB The photochem. of 2-halo-N-pyridinylbenzamide I (R = H, Cl, Br; R1 = H, Me; R2 = 4-N-(4-pyridynyl), 3-N-(3-pyridynyl), 2-N-(2-pyridynyl)) and chlorobenzanilide I (R = Cl, R1 = H, R2 = CH) was studied in aq. acetonitrile. The photoreaction of 2-chloro-N-pyridinylbenzamides produced photocyclized products, benzo[c]naphthyridinones in high yield, whereas the bromo analogs produced extensively photoreduced products, N-pyridinylbenzamides with minor photocyclized product. Since the photocyclization reaction of 2-chloro-N-pyridinylbenzamide was retarded by the presence of oxygen and sensitized by the presence of a triplet sensitizer, acetone or acetophenone, a triplet state of the chloro analog was involved in the reaction. Since several radical intermediates, particularly n-complexes of chlorine radical, were identified in the laser flash photolysis of 2-chloro-N-pyridinylbenzamide, an intramol. cyclization mechanism of Ph radical assisted with n-complexation of chlorine radical for the cyclization reaction was proposed: the triplet state (78 kcal/mol) of the chloro analog, which was populated by the excitation underwent a homolytic cleavage of the C-Cl bond to give Ph and chlorine radicals; while chlorine radical holded the neighbor pyridinyl ring with its n-complexation, the intramol. arylation of the Ph radical with the pyridinyl ring proceeded to produce a conjugated 2,3-dihydropyridinyl radical and then the conjugated radical aromatized to afford a cyclized product, benzo[c]naphthyridinone by ejecting a hydrogen. The photoredn. product can be formed by hydrogen atom abstraction of the Ph .sigma. radical from the environment.
IT **53439-83-1P**, Benzo[c][1,6]naphthyridin-6(5H)-one
338951-18-1P, 5-Methyl)-benzo[c][1,6]naphthyridin-6(5H)-one
RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(cyclized photoproduct; photolysis of halopyridinylbenzamide derivs.)

RN 53439-83-1 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one (9CI) (CA INDEX NAME)

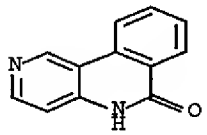


RN 338951-18-1 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one, 5-methyl- (9CI) (CA INDEX NAME)

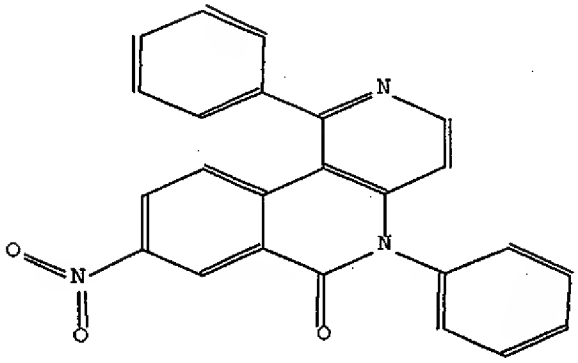


RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1974:519509 CAPLUS
DN 81:119509
TI Photoinduced reactions. XIV. Photochemistry of the amide system. IV. Photoreactions of benzoylaminopyridines
AU Itoh, Kazuhiko; Kanaoka, Yuichi
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, Japan
SO Chemical & Pharmaceutical Bulletin (1974), 22(6), 1431-2
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB Photolytic Fries rearrangement of I (x = 2) gave II (x, y = 3,2; 5,2) and III; I(x = 3) gave II (x, y = 2,3; 4,3; 2,5); I (x = 4) gave IV. III and IV were formed by cyclization while II were formed by radical dissocn. and recombination.
IT **53439-83-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 53439-83-1 CAPLUS
CN Benzo[c][1,6]naphthyridin-6(5H)-one (9CI) (CA INDEX NAME)



L8 ANSWER 1 OF 2 BEILSTEIN COPYRIGHT 2003 BEILSTEIN MDL on STN



Reference(s):

1. Vales, Magali; Lokshin, Vladimir; Pepe, Gerard; Samat, Andre; Guglielmetti, Robert, Synthesis, CODEN: SYNTBF(16), <2001>, 2419 - 2426; BABS-6325647

L8 ANSWER 2 OF 2 BEILSTEIN COPYRIGHT 2003 BEILSTEIN MDL on STN

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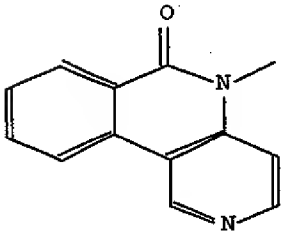
Autonom Name (AUN):	5-methyl-5H-benzo<c><1,6>naphthyridin-6-one
Molec. Formula (MF):	C13 H10 N2 O
Molecular Weight (MW):	210.23
Lawson Number (LN):	28733, 2817
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	7420294
Tautomer ID (TAUTID):	8242325
Entry Date (DED):	2001/07/25
Update Date (DUPD):	2001/07/25



Reference(s):

1. Park, Yong-Tae; Jung, Chang-Hee; Kim, Moon-Sub; Kim, Kwang-Wook, J.Org.Chem., CODEN: JOCEAH, 66(7), <2001>, 2197 - 2206; BABS-6278584

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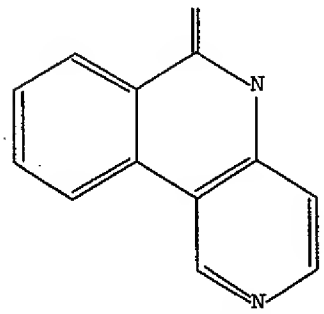


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L3              5 S L1 FUL

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L8              2 S L6 NOT L4

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FULL ESTIMATED COST                                  104.55      368.34

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